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Ischemic Threshold During Two Exercise Testing Protocols and During Ambulatory Electrocardiographic Monitoring

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Objectives. **The aim of this study was to examine the dependence of the ischemic threshold during exercise testing on the exercise protocol employed and to determine the relation between the ischemic thresholds observed during exercise and during daily activity.**

Background. **The ischemic threshold (heart rate at 1-mm ST segment depression) during daily activity has been reported to be lower than that observed during exercise testing. Recent reports have hypothesized that this difference is probably dependent on the exercise protocol employed.**

Methods. **Twenty-two patients with known coronary artery disease, not receiving antianginal medications, were evaluated by repeated exercise testing according to the Bruce and the modified Davidson protocols and by 48-h ambulatory electrocardiographic monitoring.**

Results. **Although the heart rate at 1-mm ST segment depression was somewhat lower with the Davidson than with the Bruce protocol (112 ± 14 vs. 115 ± 1[illegible] beats/min), the rate-pressure product at 1-mm ST segment depression was similar during the two protocols (16,900 ± 4,000 vs. 17,700 ± 3,600). The mean heart rate (100 + 12 beats/min) at 1-mm ST segment depression during ambulatory ischemic episodes (n = 137) was significantly lower than that observed during both exercise protocols ($p < 0.001$ for both comparisons).**

Conclusions. **Exercise-induced ischemia occurs at a relatively fixed threshold that is mainly dependent on myocardial oxygen demand and is independent of the exercise protocol employed. Ischemia on ambulatory monitoring, however, occurs at a much more variable threshold that is commonly lower than that observed during exercise and is therefore dependent on other factors in addition to increased demand.**

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Exercise testing and ambulatory electrocardiographic (ECG) monitoring are commonly used to detect and evaluate ischemia in patients with suspected or proved coronary artery disease (1–8). One main objective in using these procedures in such evaluation is to estimate the severity of ischemia for therapeutic and prognostic purposes (9–12). Ambulatory ischemia has been shown to be more prevalent in patients who exhibit exercise-induced ischemia at low versus higher work loads (9,13,14). However, among patients who exhibit ischemia on both exercise testing and ambulatory ECG monitoring, most indexes of ischemia on the two tests correlate weakly, except for heart rate at the onset of ischemia (15). This ischemic variable on Bruce protocol exercise testing has been shown to have a significant correlation with that on ambulatory monitoring, yet it has been consistently higher during exercise than during ambulatory ischemia.

Recent reports (16–18) have hypothesized that this difference in ischemic heart rate between exercise testing and ambulatory ECG monitoring is probably dependent on the exercise protocol and that the ischemic threshold observed may be lower during a gradually increasing work load protocol than during a more abruptly increasing work load protocol. However, others (19–24) have reported different findings.

The purpose of this study was to examine the dependence of the ischemic threshold during exercise on the exercise protocol used and to determine the relation between the exercise and the ambulatory ischemic thresholds in patients with stable coronary artery disease who have ischemic changes on both tests.

Methods

Study patients. Twenty-two patients with known coronary artery disease, positive findings on an exercise test and ≥2 ischemic episodes during 24 h of ambulatory ECG monitoring were studied while they were receiving no antianginal medications. There were 19 men and 3 women, 44 to 77 years old (mean 63 ± 8). The diagnosis of coronary artery disease was established according to one or more of the following criteria: 1) angiographic findings of significant coronary disease (>70% stenosis in at least one major coronary artery) in 16 patients, 2) previous myocardial infarction in 5, 3) and typical effort-induced angina in 17. The

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six patients who did not have angiographic documentation of coronary disease had scintigraphic exercise-induced reversible thallium-201 defects. Patients were excluded if their baseline ECG at rest exhibited ST-T wave changes or conduction abnormalities.

Study design. All patients performed two exercise tests according to the standard Bruce protocol and two exercise tests according to a modified Davidson protocol (25) and underwent 48-h ambulatory ECG recording within 7 days. All oral antianginal medications were withdrawn ≥48 h before the study period, and only sublingual nitroglycerin was allowed. The four exercise tests were performed during the late morning hours by all patients. Treadmill testing according to the Davidson protocol was performed twice, on the 1st and 5th days of the week, and Bruce protocol exercise testing was performed twice, on the 2nd and 6th days of the week. Forty-eight-hour ambulatory ECG recording was performed on the 3rd and 4th days of the week. The study protocol was approved by the Institutional Committee on Human Research. Patients' personal physicians gave their consent to stop all oral antianginal medications for the study period, and all patients gave informed consent to participate in the study.

Exercise testing. Treadmill testing was performed on a Quinton 3000 treadmill system. The modified Davidson protocol consisted of successive 2-min stages with a constant treadmill speed of 2 miles/h and a treadmill grade that started at 0% and increased by 3.5% at every stage. Leads aVF, V_3 and V_5 were continuously monitored and recorded every 15 s, and blood pressure was measured every minute using an electronic sphygmomanometer. A 12-lead ECG was recorded every 30 s to accurately detect the exercise time and heart rate at 1-mm ST segment depression. During the recovery period, a 12-lead ECG and blood pressure were recorded every minute for at least 7 min or until ischemic ECG changes disappeared. Patients were instructed to exercise until limited by severe chest pain, dyspnea or fatigue. In addition, exercise was stopped if ST depression was >3 mm, there was a ≥20-mm Hg decrease in systolic blood pressure or the age-adjusted maximal predicted heart rate was achieved. The exercise test was judged positive for ischemia if ≥1 mm of horizontal or down sloping ST depression, measured 80 ms after the J point, was observed in at least two ECG leads. The following exercise variables were recorded in each patient: 1) the total duration of exercise; 2) the time, heart rate, systolic blood pressure and rate-pressure product at 1-mm ST depression; 3) the heart rate, blood pressure and rate-pressure product at peak exercise; 4) the maximal transient ST depression in any ECG lead; and 5) the presence or absence of typical chest pain. The heart rate at 1-mm ST segment depression was independently determined by three observers who were aware of the exercise protocol. Differences in interpretation were resolved by consensus calls.

Ambulatory electrocardiographic monitoring. Ambulatory ECG monitoring was performed for 48 h using the ACS reel to reel two-channel AM recorders calibrated to 10 mm/1 mV and equipped with an event button. Silver-silver chloride skin electrodes were attached to the chest wall with the exploring electrodes in the V_3-like and V_5-like positions (26). The CardioData Prodigy system, combined with a PDP 11/73 computer was used for the digitization and analysis of the Holter tapes. Holter data were analyzed by a highly experienced technician using a validated computer algorithm (version 7.10) for ST segment analysis (27). The ST analysis was performed in both channels in a semiautomatic interactive method. Electrocardiographic samples were printed out in real time and visually verified by a physician who also reviewed the corresponding heart rate and ST trend histograms. An ischemic episode was defined as a transient of ≥1 mm, horizontal or downsloping depression of the ST segment lasting for ≥1 min before returning to baseline. The following Holter ischemic variables were recorded for 48 h in each patient: 1) the number of ischemic episodes; 2) the total duration of ischemia; 3) the maximal ST depression observed in any channel; 4) and the minimal, maximal and average heart rate at 1-mm ST depression.

Statistical analysis. Reproducibility of exercise test results by exercise protocol was determined by the Pearson product-moment correlation coefficient. The results of the two exercise protocols were compared using a two-factor repeated measures analysis of variance model. The two factors were exercise protocol and the day sequence of the test (nested within protocol). Heart rate increments during exercise by exercise protocol were compared using a similar model. The average heart rate at 1-mm ST depression, observed during each of the two exercise protocols, was compared with the average heart rate at 1-mm ST depression during ambulatory monitoring using the paired Student t test. A two-tailed p value < 0.05 was considered statistically significant.

Results

Reproducibility of exercise test results. The results of the two exercise tests performed according to each exercise protocol are presented in Tables 1 and 2 for the modified Davidson protocol and the Bruce protocol, respectively. Only total exercise duration and the time to 1-mm ST segment depression differed significantly between the first and second tests performed according to the Davidson protocol (Table 1). Exercise duration was longer during the second than during the first (12 ± 4.8 vs. 10.7 ± 4.5 min, respectively, p = 0.023), and the time to 1-mm ST segment depression was also longer (8.8 ± 4.6 vs. 7.7 ± 4.9 min, respectively, p = 0.018). During the two Bruce protocol exercise tests, only the time to 1-mm ST segment depression differed significantly between tests (Table 2); this variable was more prolonged during the second than during the first test (5.1 ± 2.5 vs. 4.5 ± 2.2 min, respectively, p = 0.021). The reproducibility of six exercise ischemic variables by exercise protocol is outlined in Table 3. All ischemic vari-

Table 1. Comparison of Two Exercise Tests Performed by 22 Patients 4 Days Apart Using the Davidson Protocol

Exercise Variable	Exercise Test	
	First	Second
Heart rate at rest (beats/min)	66 ± 9	65 ± 10
SBP at rest (mm Hg)	124 ± 17	126 ± 16
Maximal heart rate (beats/min)	123 ± 17	123 ± 15
MPHR achieved (%)	81 ± 13	81 ± 10
Maximal SBP (mm Hg)	161 ± 29	159 ± 26
Maximal RPP/1,000 (mm Hg × beats/min)	20.0 ± 5.3	19.8 ± 4.9
Exercise duration (min)	10.7 ± 4.5	12.0 ± 4.8*
Maximal ST↓ (mm)	1.7 ± 0.7	1.6 ± 0.6
Time to 1-mm ST↓ (min)	7.7 ± 4.9	8.8 ± 4.6†
Heart rate at 1-mm ST↓ (beats/min)	110 ± 15	112 ± 15
SBP at 1-mm ST↓ (mm Hg)	150 ± 26	153 ± 23
RPP at 1-mm ST↓/1,000 (mm Hg × beats/min)	16.6 ± 4.3	17.2 ± 4.1

*p = 0.023, †p = 0.018 comparing the two tests. Data are expressed as mean value ± SD. MPHR = maximal predicted heart rate; RPP = rate-pressure product; SBP = systolic blood pressure; ST↓ = ST segment depression.

ables had moderately high (>0.61) correlation coefficients, whereas the most reproducible ischemic variable during both exercise protocols was the time to 1-mm ST segment depression ($r = 0.91$, $r = 0.87$ for the Davidson and the Bruce protocol, respectively). The heart rate at 1-mm ST segment depression had a high coefficient for both protocols ($r > 0.8$), as did the rate-pressure product at 1-mm ST segment depression ($r > 0.77$). Overall, the r values for the six ischemic variables were similar for both protocols.

Comparison of exercise test results by exercise protocol. Because of the overall high reproducibility of ischemic variables for both exercise protocols, the results of the two protocols were first compared after averaging the results of the two tests performed according to each protocol (Table 4). Patients exercised for a longer period during the Davidson than during the Bruce protocol exercise test (11.4 ± 4.5 vs. 7.3 ± 2.1 min, respectively) and exhibited 1-mm ST segment depression later during exercise (8.3 ± 4.7 vs. 4.8 ± 2.3 min, respectively). The maximal heart rate achieved during exercise was higher in both absolute and relative terms during the Bruce than during the Davidson protocol, as was the maximal rate-pressure product (22,000 ± 4,500 vs. 19,900 ± 4,800 mm Hg × beats/min, respectively), whereas the maximal systolic blood pressure achieved was similar during both protocols. However, although the heart rate at 1-mm ST segment depression was somewhat higher during the Bruce than during the Davidson protocol (115 ± 14 vs. 112 ± 14 beats/min, respectively), the rate-pressure product at 1-mm ST segment depression during both protocols was similar (17,700 ± 3,600 vs. 16,900 ± 4,000 mm Hg × beats/min, respectively). Repeated measures analysis of variance using exercise protocol and the day sequence of the test (nested within protocol) as factors revealed protocol-related significant differences ($p = 0.0036$) in the heart rate at 1-mm ST segment depression after adjustment for the day sequence of the test ($p = 0.74$) and its interaction with the exercise protocol ($p = 0.06$). However, a similar model that was constructed for the ischemic rate-pressure product did

Table 2. Comparison of Two Exercise Tests Performed by 22 Patients 4 Days Apart Using the Bruce Protocol

Exercise Variable	Exercise Test	
	First	Second
Heart rate at rest (beats/min)	68 ± 12	65 ± 9
SBP at rest (mm Hg)	123 ± 17	129 ± 19
Maximal heart rate (beats/min)	136 ± 15	133 ± 15
MPHR achieved (%)	88 ± 10	87 ± 11
Maximal SBP (mm Hg)	162 ± 24	163 ± 27
Maximal RPP/1,000 (mm Hg × beats/min)	22.0 ± 4.4	22.0 ± 5.2
Exercise duration (min)	7.2 ± 2.3	7.3 ± 2.2
Maximal ST↓ (mm)	1.8 ± 0.6	1.9 ± 0.7
Time to 1-mm ST↓ (min)	4.5 ± 2.2	5.1 ± 2.5*
Heart rate at 1-mm ST↓	117 ± 15	114 ± 14
SBP at 1-mm ST↓	153 ± 20	152 ± 21
RPP at 1-mm ST↓/1,000 (mm Hg × beats/min)	17.9 ± 3.9	17.4 ± 3.8

*p = 0.021 comparing the two tests. Data are expressed as mean value ± SD. Abbreviations as in Table 1.

Table 3. Reproducibility Comparison of Ischemic Variables in the Two Exercise Protocols

Ischemic Variable	r Value	
	Davidson Protocol	Bruce Protocol
Exercise duration	0.86	0.78
Maximal ST↓	0.74	0.80
Time to 1-mm ST↓	0.91	0.87
Heart rate at 1-mm ST↓	0.81	0.86
SBP at 1-mm ST↓	0.73	0.61
RPP at 1-mm ST↓	0.78	0.79

Abbreviations as in Table 1.

Table 4. Comparison of Exercise Testing Results by Exercise Protocol in 22 Patients

Exercise Variable	Exercise Protocol	
	Bruce	Davidson
Heart rate at rest (beats/min)	66 ± 9	66 ± 8
SBP at rest (mm Hg)	126 ± 16	125 ± 14
Maximal heart rate (beats/min)	135 ± 14	123 ± 15
MPHR achieved (%)	88 ± 9	81 ± 11
Maximal SBP (mm Hg)	162 ± 23	160 ± 27
Maximal RPP/1,000 (mm Hg × beats/min)	22.0 ± 4.5	19.9 ± 4.8
Exercise duration (min)	7.3 ± 2.1	11.4 ± 4.5
Maximal ST↓ (mm)	1.8 ± 0.6	1.7 ± 0.6
Time to 1-mm ST↓ (min)	4.8 ± 2.3	8.3 ± 4.7
Heart rate at 1-mm ST↓ (beats/min)	115 ± 14	112 ± 14
SBP at 1-mm ST↓ (mm Hg)	152 ± 19	151 ± 23
RPP at 1-mm ST↓/1,000 (mm Hg × beats/min)	17.7 ± 3.6	16.9 ± 4.0

Values are expressed as mean value ± SD. Abbreviations as in Table 1.

Table 5. Summary of Results of 48-Hour Ambulatory Electrocardiographic Monitoring in 22 Patients

Variable	Range	Mean ± SD
Ischemic episodes (n)	1 to 19	6.1 ± 4.5
Symptomatic episodes (%)	0 to 78	15 ± 23
Total ischemia duration (min)	2.5 to 257	39 ± 57
Maximal ST depression (mm)	1 to 6	2.6 ± 1.3
Heart rate at 1-mm ST depression (beats/min)		
Minimal	57 to 111	89 ± 14
Maximal	85 to 144	111 ± 15
Mean	77 to 121	100 ± 12

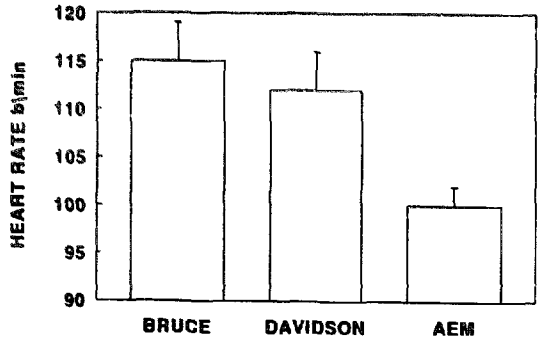
not detect protocol- or day sequence–related significant differences in this variable ($p = 0.16$).

Ambulatory electrocardiographic monitoring results. During 1,056 h of ambulatory ECG monitoring in 22 patients, 137 ischemic episodes were recorded. Table 5 summarizes the ambulatory ECG monitoring results for the 22 patients. The mean number of ischemic episodes was 6.1 ± 4.5 (range 1 to 19), and only 15% of these episodes were symptomatic. Total ischemia duration was 2.5 to 257 min (mean 39 ± 57), and the mean maximal ST segment depression observed was 2.6 ± 1.3 mm.

The heart rate at 1-mm ST depression (ischemic threshold) during ischemic episodes was quite variable (57 to 144 beats/min) and averaged 100 ± 12 beats/min per patient.

Ischemic threshold during ambulatory electrocardiographic and during exercise. A comparison of the mean heart rate at 1-mm ST segment depression during ambulatory ECG monitoring with that observed during each of the two exercise protocols employed in 22 patients is depicted in Figure 1. As can be seen, the mean ischemic threshold during ambulatory ECG monitoring was significantly lower ($p < 0.001$) than that observed during both the Bruce protocol and the Davidson protocol exercise tests. The difference between the mean ischemic threshold on the two exercise protocols (3 beats/min) was significantly smaller ($p < 0.01$) than the difference between the mean ischemic

Figure 1. Mean heart rate at 1-mm ST segment depression during 2 exercise protocols (Bruce and Davidson) and during ambulatory electrocardiographic monitoring (AEM). Vertical bars indicate 1 SD. b = beats.



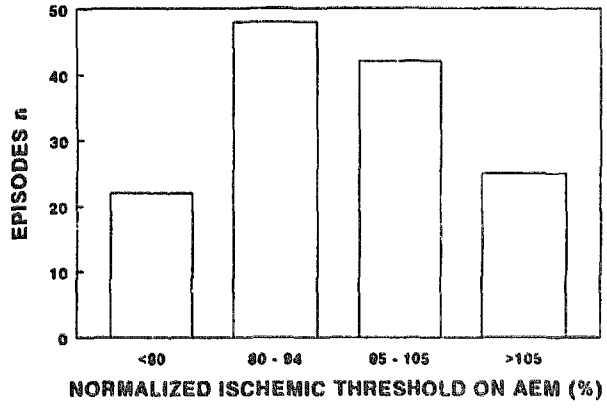


Figure 2. Frequency distribution of the mean heart rate at 1-mm ST segment depression during ambulatory electrocardiographic monitoring (AEM) normalized by patient to the heart rate at 1-mm ST segment depression during a Davidson protocol exercise test. EPISODES = number of ischemic episodes.

threshold on ambulatory ECG monitoring and that on each of the exercise protocols employed (15 beats/min for the Bruce protocol and 12 beats/min for the Davidson protocol). To better describe the relation between the ischemic threshold on ambulatory ECG monitoring to that during exercise, the ischemic threshold during each ischemic episode on ambulatory ECG monitoring was normalized to the corresponding ischemic threshold on the Davidson exercise protocol in the same patient. The frequency distribution of this normalized ambulatory ECG monitoring ischemic threshold for the 137 ischemic episodes is depicted in Figure 2. The ischemic threshold during ambulatory ECG monitoring had a mean value equivalent to 94 ± 13% of the ischemic threshold on the Davidson protocol exercise test (range 58% to 133%). However, the frequency distribution of the normalized ischemic threshold was significantly ($p < 0.05$) shifted to the left of 100%: 1) 42 ischemic episodes (30%) had an ischemic threshold that was 95% to 105% of the ischemic threshold during the Davidson protocol exercise test (that is, a similar threshold); 2) only 25 episodes (18%) had an ischemic threshold >105% of the exercise ischemic threshold; and 3) 70 episodes had an ischemic threshold that was <95% of the exercise threshold. Despite this apparent shift to the left of the frequency distribution, nearly half (48%) of the ambulatory ischemic episodes occurred at an ischemic threshold that was similar to or greater than the ischemic threshold on the Davidson protocol exercise test.

Discussion

The main findings of this study indicate that the ischemic threshold during exercise treadmill testing is independent of the exercise protocol employed: the mean rate-pressure product at 1-mm ST segment depression was not significantly different on both protocols (17,700 ± 3,600 on the Bruce and 16,900 ± 4,000 mm Hg × beats/min on the

Davidson protocol) even after adjustment for the day sequence of the test and its interaction with the exercise protocol employed. The mean heart rate at 1-mm ST segment depression was slightly higher on the Bruce than on the Davidson exercise protocol (115 ± 14 vs. 112 + 14 beats/min, respectively), yet it was significantly higher during both exercise protocols than during ambulatory ischemic episodes in the same patients (100 ± 12 beats/min). Thus, exercise-induced ischemia occurs at a relatively fixed threshold that is mainly dependent on myocardial oxygen demand and is independent of the exercise protocol. However, ischemia during ambulatory ECG monitoring occurs at a much more variable threshold that is usually lower than that observed during exercise in the same patient and therefore is dependent on other factors in addition to myocardial oxygen demand. Among these other factors, the most important one is probably myocardial oxygen supply that can be modified by changes in coronary tone.

Methodologic considerations. *Training effect.* We carried out two exercise tests according to each protocol to account for the possible training effect that could take place during short-term repeated exercise testing, and indeed a training effect was apparent on both protocols (Tables 1 and 2). Total exercise duration was significantly longer during the second than during the first Davidson protocol test (12 ± 4.8 vs. 10.7 ± 4.5 min), as well as the time to 1-mm ST segment depression (8.8 ± 4.6 vs. 7.7 ± 4.9 min). Similar findings regarding the time to 1-mm ST segment depression on the two Bruce protocol tests were obtained. The exercise protocol effect on the ischemic threshold was adjusted for the day sequence of the test in the two-factor repeated measures analysis of variance. However, we have not completely excluded a training effect because both of the Bruce exercise tests were consistently performed 1 day after the Davidson tests.

Frequency of electrocardiographic recordings during exercise. To accurately determine the heart rate at 1-mm ST segment depression during exercise, one must record frequent ECGs especially when using an exercise protocol like the Bruce protocol that results in relatively abrupt changes in heart rate. We therefore, recorded a 12-lead ECG every 30 s, and in some instances we recorded a 3-lead ECG in-between successive 12-lead recordings. Figure 3 depicts the heart rate changes during exercise by the exercise protocol employed in the present study. As can be seen, the Bruce protocol resulted in much more prominent and abrupt heart rate increments than did the Davidson protocol. Repeated measures analysis of variance using exercise protocol and the day sequence of the test (nested within protocol) as factors revealed highly significant ($p < 0.001$) protocol-related differences in heart rate changes during exercise after adjustment for the day sequence effect. It is obvious that when a serial ECG recording is delayed beyond the point of 1-mm ST segment depression during the course of an exercise test, the subsequent determination of the heart rate at 1-mm ST depression will be affected by a systematic error toward a higher value. We believe that this might be the principal reason for the slight but significant difference we found between the heart rate at 1-mm ST depression during the two exercise protocols used. However, other reasons for this difference cannot be excluded. The fixed sequence of the two protocols (Bruce test performed 1 day after the Davidson test) could also explain the higher heart rate at 1-mm ST depression on the Bruce protocol.

Concomitant use of antianginal medications. To avoid any surrogate effects that might be produced by the concomitant use of antianginal medications, in the present study no antianginal medications were given to any patients during the whole study period.

Ischemic threshold during exercise by exercise protocol. Our results agree with previous studies that have found a relatively fixed ischemic threshold during repeated multiprotocol stress testing (19–24). However, they contrast with recent findings reported by others (16–18). Garber et al. (17) studied 33 patients with known coronary artery disease by the Bruce protocol and a submaximal steady state protocol. Their results indicate that the ischemic threshold in terms of the rate-pressure product at 1-mm ST segment depression can be lower during a submaximal protocol than during the Bruce protocol. Their patient group was similar to the present study group with regard to the average ischemic threshold during exercise. However, several methodologic differences exist between the two studies. Garber et al. (17) administered each treadmill protocol only once, 2 to 7 days apart and not in a random order; in addition, they recorded a 12-lead ECG only every 60 s and did not withdraw oral antianginal medications for the study period. Panza et al. (18) reported their experience with 47 patients with stable coronary artery disease who had reproducible ischemia during repeated exercise testing using the Bruce and the National Institutes of Health (NIH) combined exercise protocols. They reported a significantly higher heart rate at 1-mm ST segment depression during the Bruce than during the NIH combined exercise protocol (126 ± 16 vs. 112 ± 9, respectively, $p < 0.0001$). However, a 12-lead ECG was recorded only every 60 s during both exercise protocols even though heart rate increments were significantly more prominent during the Bruce than during the NIH combined protocol ($p < 0.0001$). In addition, each exercise protocol was performed only once, and the period between the two exercise tests varied between 3 to 30 days. Panza et al. (18) also did not report the rate-pressure product at 1-mm ST segment depression during the two exercise protocols used in their study.

Ischemic threshold during exercise and during ambulatory electrocardiographic monitoring. Our results indicate that the mean heart rate at 1-mm ST segment depression during ambulatory monitoring was significantly lower than that observed during the Bruce and the Davidson exercise protocols. In a previous study (15) of 60 patients with stable coronary artery disease not receiving antianginal medications we demonstrated that the mean heart rate at 1-mm ST

segment depression during ambulatory ischemic episodes was significantly lower than that observed during a Bruce protocol exercise test. Other studies (28) have reported similar findings, whereas Panza et al. (18) reported similar findings for the Bruce but not for the NIH combined protocol. As mentioned previously, Panza et al. determined the heart rate at 1-mm ST segment depression during exercise according to relatively infrequent (every minute) ECGs. In our study, frequent (every 30 s) ECG recordings during exercise demonstrated that the heart rate at 1-mm ST segment depression was significantly higher during both exercise tests than during ambulatory monitoring. Moreover, after normalizing the heart rate at 1-mm ST segment depression on ambulatory ECG monitoring to the heart rate at 1-mm/ST segment depression on the Davidson protocol for each ambulatory ischemic episode, the frequency distribution of this normalized ischemic heart rate was significantly shifted to the left of 100% (Fig. 2). This frequency distribution better represents the variability/patient of the ischemic threshold during ambulatory monitoring and the fact that the ischemic threshold on ambulatory monitoring is commonly lower than that on exercise.

Limitations. Our study design included two treadmill test pairs according to two exercise protocols, each performed 4 days apart within the same week. Because we wanted to keep a constant period between each pair of tests, we had to schedule the two exercise protocols alternately twice. According to this scheme, the Davidson protocol test was scheduled for the 1st and 5th days, whereas the Bruce protocol test was performed on the 2nd and 6th days of the study. This procedure might have caused a greater training effect in the Bruce protocol tests than in the Davidson protocol tests.

Because our patient group included only patients with ischemia during both ambulatory monitoring and exercise, it is possible that our results are applicable only to this selected group of patients. However, because previous studies that did not select their patients according to the presence of ambulatory ischemia also found that the ischemic threshold did not depend on the exercise protocol (19–24), our results are probably applicable to a larger patient group. Electrocardiograms were recorded in our study at a moderately high frequency. However, because our results clearly demonstrated that frequent electrocardiogram recordings are essential for accurate determination of the ischemic threshold (Fig. 3), we recommend continuous electrocardiogram recording during exercise for future studies of this sort. Such studies might also consider using comparable leads and monitoring equipment during stress testing and during ambulatory monitoring, as previously reported (26).

Conclusions. This study demonstrates that the ischemic threshold during exercise is independent of the exercise protocol used and therefore implies that exercise-induced ischemia is mainly dependent on an increase in myocardial oxygen demand in the setting of relatively fixed coronary stenoses. However, ambulatory ischemic episodes occur at a more variable threshold that is commonly significantly lower than the threshold observed during exercise. Therefore, ischemia recorded by ambulatory monitoring probably involves mechanisms in addition to increase in myocardial oxygen demand.

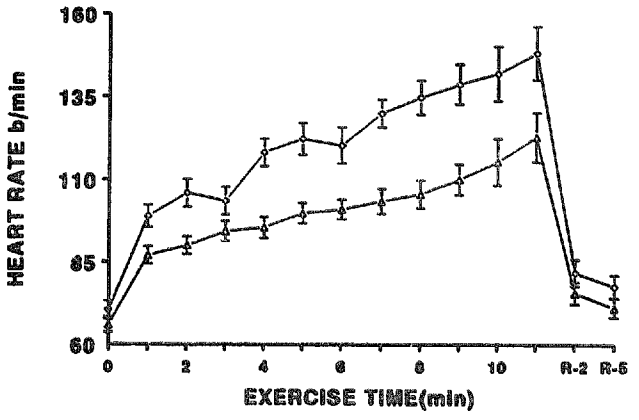


Figure 3. Heart rate changes versus exercise time during Davidson (lower curve) and Bruce (upper curve) exercise protocols in 22 patients. Vertical bars indicate SEM. b = beats; R-2 = 2-min recovery; R-5 = 5-min recovery.

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